REMARKS

Status of the Claims

Claims 1, 3-31, 34 and 35 are pending. Claims 3, 13, 14, and 26-30 stand withdrawn. Claims 1, 4-12, 15, 16, 31, 34, and 35 stand rejected. Claims 17-25 are not rejected and thus are believed to be allowable.

Summary of Board's Decisions

On September 14, 2011, the Board issued a decision affirming the USPTO's obviousness rejection of claims 1, 4-12, 15, 16, 31, 34, and 35, but reversing the obviousness rejection over claims 17-25. In affirming the obviousness rejection, the Board contends that, *inter alia*, the specification's results in Figure 8 were not unexpected because the data "supports a conclusion that the increase in proliferation was additive."[1]

Appellants requested a rehearing of the Board's decision. Appellants' argued that (1) the Board did not consider the relative increase in proliferation of the test groups compared to the control group; and (2) when properly considered, one of skill in the art would have concluded that the results are not simply additive, but synergistic and unexpected.[2] Appellants also pointed out that the Board's comments regarding the purported "additive" effect was not previously raised by the USPTO and thus constituted a new rejection.[3]

The Board agreed that its "analysis differs from the Examiner's and properly constitutes a new ground of rejection."[4] Accordingly, under 37 C.F.R. § 41.50(b), Appellants submit a response to this new rejection with new evidence for reconsideration by the USPTO.

Rejections under 35 U.S.C. 103(a)

Claims 1, 4-12, 15, 16, and 31 stand rejected as allegedly being obvious Adachi, Sutterlüty, Sherr"); Flink, and Poolman.[5]

Appellants respectfully traverse.

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[1] Board Decision, mailed September 19, 2011, page 6.

[2] Request for Rehearing, pages 2 and 3.

[3] *Id.* at pages 2, 4, and 5.

[4] Decision, page 2.

[5] The full citations of all references cited herein are of already record.

To support Appellants' unexpected results argument, a Declaration Under § 1.132 by Dr. Hiromitsu Takagi ("Takagi Dec."), one of the instant inventors,[6] is submitted herewith.

Dr. Takagi explains that Example 4 teaches the introduction of (1) a cyclin D and a CDK4 gene; (2) a cyclin gene, a CDK4 gene, and a Skp2 gene; (3) a Skp2 gene alone; and (4) a control vector into cardiomyocytes.[7] Dr. Takagi states that the results of this experiment are described in Example 4 and Figure 8, and can be represented as follows:[8]

Group	**Increase in Proliferation (observed after 7 days of culture)**	**Increase in Group Compared to Control (Group - Control) = increase in proliferation (folds)**
Control	1.8	0
Skp2	2.0	.2
D1+CDK4	3.2	1.4
D1+CDK4+Skp2	5.3	**3.5**

These results show that when (1) a cyclin D and CDK4 gene; and (2) Skp2 gene alone are introduced into a cardiomyocyte, a 1.4 fold and .2 fold increase in proliferation are observed compared to a control, respectively.[9] Dr. Takagi concludes that, using these numbers, one of ordinary skill in the art would have expected a 1.6 fold increase of proliferation if a cyclin D, CDK4 gene, and Skp2 gene were introduced into cardiomyocytes compared to the control.[10] However, when a cyclin gene, a CDK4 gene, and a Skp2 gene were introduced into a cardiomyocyte, a 3.5 fold increase in proliferation was observed.[11] Dr. Takagi concludes that this significant increase in proliferation was surprising and unexpected.[12]

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[6] *See* Takagi Dec., ¶¶ 1-5 (describing, *inter alia*, Dr. Takagi's academic and professional experience).

[7] *Id.* at ¶ 6.

[8] *Id.*

[9] *Id.* at ¶ 7.

[10] *Id.*

[11] *Id.* at ¶ 8.

[12] *Id.*

A similar result was observed in Example 5.[13] Dr. Takagi explains that Example 5 teaches the introduction of (1) a cyclin D and a CDK4 gene; (2) a cyclin gene, a CDK4 gene, and a siRNA specific to the $p27^{Kip1}$ gene ("p27 siRNA"); (3) a p27 siRNA alone; and (4) a LacZ expression virus (control vector) into cardiomyocytes.[14] Dr. Takagi states that the results are described in Example 5 and Figure 10 and can be represented as follows:[15]

Group	Increase in Proliferation (observed after 7 days of culture)	Increase in Group Compared to Control (Group - Control) = increase in proliferation (folds)
Control	1.2	0
Skp2	1.3	.1
D1+CDK4	2.8	1.6
D1+CDK4+ p27 siRNA	4.6	**3.3**

These results show that when (1) a cyclin D and CDK4 gene; and (2) p27 siRNA alone are introduced into a cardiomyocyte, a 1.6 fold and .1 fold increase in proliferation are observed compared to a control, respectively.[16] Dr. Takagi concludes that, using these numbers, one of ordinary skill in the art would have expected a 1.7 fold increase of proliferation if a cyclin D, CDK4 gene, and p27 siRNA were introduced into cardiomyocytes compared to the control.[17] However, when a cyclin gene, a CDK4 gene, and a p27 siRNA were introduced into a cardiomyocyte, a 3.3 fold increase in proliferation was observed.[18] Dr. Takagi concludes that this significant increase in proliferation was surprising and unexpected.[19]

In view of the specification's results and Dr. Takagi's Declaration, one of ordinary skill in the art would conclude the effect produced by introducing a cyclin, a cyclin-dependent kinase, and a

[13] *Id.* at ¶ 9.

[14] *Id.*

[15] *Id.*

[16] *Id.* at ¶ 10.

[17] *Id.*

[18] *Id.* at ¶ 11.

[19] *Id.*

gene encoding a factor that inhibits the production, function or action of Cip/Kip family protein, into cardiomyocytes, is not simply additive, but rather synergistic and unexpected. The Board's own review of the art shows that the Board viewed the "expected" results as merely achievement of an additive effect, not the synergistic effect achieved by Appellants. Accordingly, because the Board misinterpreted Appellants' evidence of unexpected results, Appellants' respectfully request that this rejection be withdrawn.

Claims 34 and 35 under 35 U.S.C. § 103(a) as being allegedly unpatentable over Adachi, Sutterlüty, Sherr, Flink, and Poolman, and further in view of Carrano.

Appellants respectfully traverse.

As discussed above, the claimed invention achieves an unexpected result. The USPTO's citation of Carrano does not affect this conclusion. Indeed, Carrano is unrelated to cardiomyocytes or methods of proliferating cardiomyocytes, and merely directs one of ordinary skill in the art to consider cell cycle mechanisms in cancer.[20] Accordingly, the rejection over claims 34 and 35 should be withdrawn.

[20] *See* Carrano, page 193, first column, first paragraph and page 198, second column, last paragraph.

CONCLUSION

Appellants respectfully submit that the claims are in condition for allowance, and such disposition is earnestly solicited. Should the Examiner believe that any issues remain after consideration of this response, she is invited to contact the Appellants' undersigned representative to discuss and resolve such issues.

This response is being filed within the time period set forth in the Decision (February 20th being a Federal Holiday). Accordingly, no fees are due. Should any fees be required to enter this response or keep this application pending, however, the USPTO is authorized to charge such fees to Deposit Account No. 50-0206.

Respectfully submitted,
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